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The Degenerate Thermal Rearrangement of 3,3-Difluoromethylenecyclobutane. The Effect of gem-Difluoro Substituents on Cyclobutane Bond Strength

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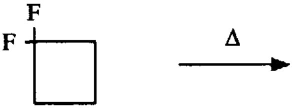
Abstract: A study of the thermal degenerate rearrangement of 3,3-difluoro-1-(dideuteriomethylene)cyclobutane indicated that the geminal CF_2 group gives rise to a 5.5 kcal/mole strengthening of the C_2-C_3 bond.

Because of our current interest in the kinetic and thermodynamic factors which are related to unimolecular, thermal rearrangements of fluorine-substituted cyclobutane and cyclobutene systems, we require specific knowledge of relative bond strengths of cyclobutane bonds which have various fluorine substitution patterns.

While the effect of fluorine substitution on the kinetic and thermodynamic stability of cyclopropanes has been studied extensively[1,2], by comparison the related influence of fluorine on the stability of cyclobutane systems has thus far attracted little attention. Certainly, it is known that perfluorocyclobutane has unusual thermal stability (E_a = 74.3 kcal/mol for cleavage compared to 62.5 kcal/mol for cyclobutane itself).[3,4] However, the related kinetic effects of lesser numbers of fluorine substituents have not been unambiguously assessed. Conlin and Frey have examined the *overall* thermal retro-(2 +2) conversions of 1,1-difluoro- and 1,1,2,2-tetrafluorocyclobutanes, **1** and **2**.[5,6] However, it is not possible from these results to unambiguously acertain the relative bond strengths of any *specific bonds* in these substrates.



$CH_2{=}CF_2 + CH_2{=}CH_2$ E_a = 69.2 kcal/mole

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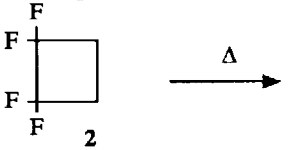
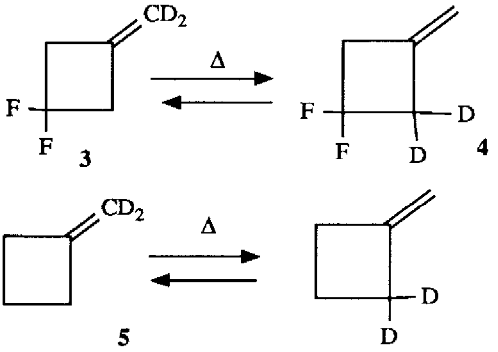


2 $CH_2{=}CF_2$ E_a = 69.8 kcal/mole

2

While we were able, in some recently reported work[7], to gain more specific insight into the tetrafluoro system, we wish now to report data pertinent to the *di*fluorocyclobutane system which was obtained via the thermal rearrangement of 3,3-difluoro-1-(dideuteriomethylene)cyclobutane, **3**. The activation enthalpy for this degenerate thermal rearrangement, relative to that for methylenecyclobutane (**5**) itself[8], should provide direct measurement of the effect of a single cyclobutane CF_2 group on the strength of its adjacent bond.



Log A = 14.1 ± 0.2

E_a = 55.0 ± 0.7 kcal/mole

Log A = 14.8 ± 0.3

E_a = 49.5 ± 1.0 kcal/mole

3,3-Difluoromethylenecyclobutane, **3**, was synthesized from 3,3-difluorocyclobutanecarboxylic acid[9] via a five step procedure which was analogous to that utilized in preparation of 1,2-bis-(dideuteriomethylene)cyclobutane.[10,11] It was found to undergo thermal rearrangement in the gas phase over the temperature range 377.7° - 444.8°C (compared to 287.5 - 354.8°C for the parent system[8]). The reaction followed good first order kinetics, and the rates at seven temperatures were determined by ^{1}H NMR integration. They are reported in the Table.

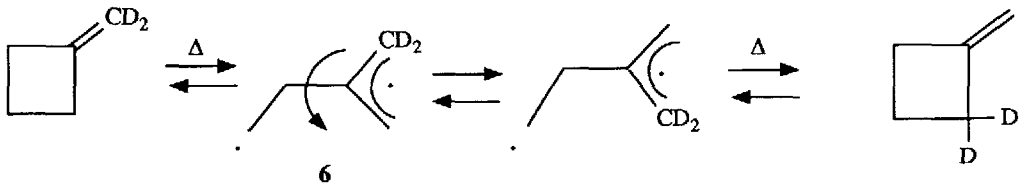
Table. Rates of Thermal Rearrangement of 3,3-Difluoro-1-(dideuteriomethyenecylobutane.

Temp.,°C	$10^4(k_1+k_{-1})$	10^4k_1[a]	10^4k_{-1}[a]
377.7	0.703 ± 0.012	0.468	0.236
382.4	0.951 ± 0.011	0.630	0.321
391.8	1.67 ± 0.03	1.11	0.558
400.9	2.75 ± 0.02	1.83	0.914
420.0	8.95 ± 0.12	5.95	3.00
432.8	20.0 ± 0.3	13.3	6.71
444.8	36.1 ± 0.4	24.0	12.1

[a] An average observed equilibrium value for $(k_1/k_{-1})_\infty$ of 1.98 was used in these calculations.

The activation parameters for the thermal interconversion of **3** and **4** were determined by a least-squares analysis of the Arrhenius plot of the rate data: for k_1: Log A = 14.1 ± 0.2, E_a = 55.0 ± 0.7 kcal/mol, with $\Delta H^{\neq}$ = 53.6kcal/mol, $\Delta S^{\neq}$ = 2.5 cal/deg, $\Delta G^{\neq}$ =52.0 kcal/mol at 407.0°C. For k_{-1}: Log A = 13.8 ± 0.2, E_a = 55.0 ± 0.7 kcal/mol, with $\Delta H^{\neq}$ =53.6 kcal/mol, $\Delta S^{\neq}$ = 1.0 cal/deg, $\Delta G^{\neq}$ = 52.9 kcal/mol at 407.0°C.

It is generally accepted that methylenecyclobutane rearrangements proceed via an initial homolysis of the C_2-C_3 bond to form an allyl ethyl diradical, **6**, which in proceeding to product rotates about the C_1-C_4 bond and then recyclizes.[12] As is generally the case in a series of related unimolecular processes where the mechanisms are assumed to be the same, in this study the observed energies of activation are considered to be an accurate measure of the relative C_2-C_3 bond strengths of **3** and **5**. Thus there is observed an apparent 5.5 kcal/mole bond *strengthening* of the C_2-C_3 bond of **3** relative to that of **5** due to the CF_2 group. This can be compared to the slight *weakening* observed (1.2 kcal/mole) when a *single* F substituent is present.[13]



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In a methylenecyclobutane rearrangement, those factors which combine to determine a particular bond strength are (a) the inherent specific bond strength of the bond undergoing homolysis (in the case of the parent **5** this can be taken to be 82 kcal/mol, the bond dissociation energy of butane's C_2-C_3 bond[14]), (b) the relief of ring-strain in the transition state (generally thought to be complete in the case of homolytic ring-cleavages, and estimated to be 27.9 kcal/mol for **5**[15]), and (c) any stabilization of the transition state due to delocalization in the incipient allyl radical (calculated using the equation below to be 5.3 kcal/mol for **5**).

$$\Delta H^{\neq} = \text{(Inherent Bond Strength)} + \text{(Ring Strain)} + \text{(allyl stabilization)}$$

Assuming that the latter effect should be identical for **3** and **5**, the end result would be that changes in $\Delta H^{\neq}$ for C_2-C_3 bond homolysis due to substituents at C_3 must derive from a difference in inherent bond strength, a difference in ring strain, or some combination thereof.

For the case of geminal difluoro substitution at C_3, *neither* the expected inherent bond strength nor the ring strain has been determined experimentally, although Smart and Dixon have estimated the CH_3CF_2-CH_2CH_3 bond dissociation energy to be 90.5 kcal/mol.[18] Inserting that number into the $\Delta H^{\neq}$ equation, one can derive a strain energy for **3** of 31.5 kcal/mol, 3.6 kcal more than that for the parent **5**. On the other hand, Smart and Dixon have also estimated the *ring strain* of difluorocyclobutane (relative to $CH_3CF_2CH_2CH_3$) to be 27.0 kcal/mol[18](as compared to a strain of 26.5 for cyclobutane itself relative to butane[19]). With methylenecyclobutane having 1.4 kcal/mol more strain than cyclobutane, one can thus estimate a ring strain for **3** to be 28.4 kcal/mol, and inserting that value into the $\Delta H^{\neq}$ equation leads to a value of 87.4 kcal/mol for the inherent RCF_2-CH_2R bond strength. This is 5.4 kcal/mol *stronger* than the bond dissociation energy for the C_2-C_3 bond of butane.

It can be seen that without the availability of accurate experimental data for either the strain energy of a 1,1-difluorocyclobutane system or for the bond dissociation energy of a model RCF_2-CH_2R bond system, one *cannot* be certain as to the reason for the observed stronger C_2-C_3 bond of **3** relative to **5**. For many purposes, however, it suffices simply to know the *net effect* of the presence of a CF_2 group in a cyclobutane ring, namely that it strengthens the adjacent CF_2-CH_2 bonds by 5.5 kcal/mol.

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